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Dermatophytes: Keratin Eaters

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ABSTRACT

Dermatophytes are a group of closely related keratinophilic fungi belonging to the anamorphic genera *Trichophyton*, *Microsporum* and *Epidermophyton*. They have the capacity to invade keratinized tissue such as skin, hair, and nails of humans and animals to produce a superficial mycotic infection called dermatophytosis. In one of the survey conducted by World Health Organization (WHO), it has been reported that about 25% people worldwide have cutaneous infections. People of all ages are affected by the dermatophytosis. Migration, climatic factors, growth in tourism, changes in socioeconomic conditions, overcrowding, healthcare, environmental hygiene, culture and individual characteristics may influence the epidemiology of dermatophytoses. There are different types of dermatophytosis and have been named according to the anatomic locations involved.. The main aim of this paper is to review the etiology, prevalence, and clinical presentation, the latest knowledge on pathogenesis of dermatomycosis. This article mainly focuses on recent published work on different aspects of dermatophytes.

Keywords: Dermatophytosis, Keratinophilic, Anthropophilic, Dermatophytes, Serology, Onychomycosis, Ringworm, Griseofulvin.

INTRODUCTION

A group of closely related keratinophilic fungi are called dermatophytes. They can invade keratinized tissues of humans and animals such as stratum corneum of skin, hair and nails causing superficial infection called dermatophytosis (Weitzman and Summerbell, 1995; Garg *et al.,* 2009). These organisms are particularly well adapted to infect this location even though they are not part of the normal human skin flora, because they have the ability to use keratin as a source of nutrients by producing extracellular enzymes named keratinases, unlike most other fungal pathogens (Wagner and Sohnle, 1995). Based on the formation and morphology of their conidia dermatophytes are classified into three genera namely *Trichophyton*, *Microsporum* and *Epidermophyton*, (Simpanya, 2000; Madhavi *et al.,* 2011; Cortez *et al.,* 2012). Each of which includes several recognized species (Roque *et al.,* 2006). Nowadays 41 species of dermatophytes were identified (Gharachorlou *et al.,* 2011). These fungi are distributed worldwide with various degrees (Coelho *et al.,* 2011; Woodfolk, 2005; Bokhari, 2009). These fungi are both keratinophillic and keratinolytic (Blanco and Garcia, 2008; Shrivastav *et al.,* 2013).

CLASSIFICATION OF DERMATOPHYTES

Dermatophytes are classified according to the genera, the ecology and patterns of infection (Palacio *et al.,* 2000).

ECOLOGICAL CLASSIFICATION

Dermatophyte species are traditionally classified into three groups based on the ecological niche in which they reside. These include geophilic species that live in soil, zoophilic species that are associated with animals, and anthropophilic species that associated with humans (Peres *et al.,* 2010; Ndako *et al.,* 2012; Summerbell, 2000; Abdo *et al.,* 2011). Some of these dermatophytes have developed host specificity probably during their evolution from their natural habitat in the soil. The difference in host specificity is because of the differences in keratin of the hosts (Simpanya, 2000).

Anthropophiles

Anthropophilic species usually infect humans but they may also infect animals. Infection transmits from man to man (Abdo *et al.,* 2011). They account for over 70% of infections in humans and can lead to a persistent illness (Peres *et al.,* 2010; Achterman and White, 2012). These fungi typically produce superficial dermatomycoses characterized by relatively low inflammatory activity. According to Havlickova et al. (2002), household dust can serve as a reservoir for antropophilic dermatophytes by retaining spores of dermatophytes for years (Havlickova *et al.,* 2002).

Zoophiles

Zoophilic species infect animals and transmission from animals to humans can occur (Simpanya, 2000;

Weitzman and Summerbell, 1995). They are pathogens with only one animal host and grow as saprophytes on animal materials. Human beings acquire the infection from infected animals (Lakshmipathy and Kannabiran, 2010). They have a high affinity to the hairy head of a child. About 30% of human dermatophytoses are caused by zoophilic organisms, which frequently cause acute inflammation and have a self-healing characteristic (Achterman and White, 2012). They are associated to skin diseases that are extremely inflammatory and maybe highly infectious (Havlickova *et al.,* 2002).

Geophiles

Geophilic species inhabit soil and infect both humans and animals. Certain species are maintained and spread by fomites (Simpanya, 2000). They are often saprophytic and obtain nutrients from keratinous substrates (Lakshmipathy and Kannabiran, 2010). They are thought to have been ancestral to the pathogenic dermatophytes, pre adapted to cutaneous pathogenesis by their ability to use keratin and their consequent close association with animals living in hair and feather-lined nests in contact with soil (Weitzman and Summerbell, 1995). These fungi only sporadically infect humans (Havlickova *et al.,* 2002).

ETIOLOGICAL AGENT

The dermatophytes consist of three anamorphic (asexual or imperfect) genera, *Epidermophyton*, *Microsporum* and *Trichophyton*. They belong to the class hyphomycetes of the Deuteromycota (Fungi Imperfecti) (Weitzman and Summerbell, 1995; Stojanov *et al.,* 2011).

Trichophyton

The genus *Trichophyton* consists of 24 species, the most frequent species include, *T. mentagrophytes, T. rubrum, T. verrucosum* and *T. violaceum.* On agar media, they form powdery, velvety or waxy colonies. *Trichophyton* species can be identified by characteristic reverse side pigmentation. For instance, the pigmentation on the reverse side of *Trichophyton rubrum* is wine red colour. Microconidia are more predominant than macroconidia (Weitzman and Summerbell, 1995; Stojanov *et al.,* 2011) . Microconidia, may be globose, pyriform or clavate, or sessile or stalked, and are formed singly along the sides of the hyphae or in grape-like clusters. They are 2-3µm in size (Simpanya , 2000) .The macroconidia are thin walled with smooth surface and cigar-shaped or pencil shaped; they may become cylindrical, or resemble a long wedge, having 1 to12 septae. They appear alone or in the group. They are 8–86 µm x 4–14 µm in size. Some species rarely produce macroconidia (Lakshmipathy and Kannabiran, 2010; Stojanov *et al.,* 2011). The type species is *T. tonsurans* (Weitzman and Summerbell, 1995; Simpanya, 2000).

Microsporum

The genus *Microsporum* consists of 16 species. The *Microsporum* species forms either white velvety or powdery colonies with yellowish brown pigmentation at the center and yellowish to brown pigmentation on the reverse of the colonies. The colonies possess radial ridges. *Microsporum* species produces both macro and microconidia (Lakshmipathy and Kannabiran, 2010; Mihali *et al.,* 2012), but the predominant conidia are macroconidia. Microconidia are less abundant. The macroconidia are multi septate (1 to 15 septa) with a thin or thick echinulate cell wall and are spindle shaped. Originally, the macroconidia were described by Emmons as spindle shaped or fusiform, obovate (egg shaped) in *Microsporum nanum* and cylindrofusiform in *Microsporum vanbreuseghemii* and may be numerous or scarce. However, the essential distinguishing feature of this genus is the presence of echinulations on macroconidial cell wall. The thickness of the cell wall and shape varies depending on the species. They range in size from 6 to 160 by 6 to 25 mm (Stojanov *et al.,* 2011).They can be stocky, with stalk or sphenoid appearance, usually individually situated along hyphae. Microconidia are pyriform, about 2-3µm in size. They are sessile or stalked. They are clavate and usually arranged singly along the hyphae or in racemes as in *Microsporum racemosum*, a rare pathogen (Weitzman and Summerbell, 1995).The type species is *M. audouinii* (Simpanya , 2000). Rarely some species produce neither micro nor macroconidia. They do not have any special nutritional requirements (Lakshmipathy and Kannabiran, 2010).

Epidermophyton

The genus *Epidermophyton* consists of only 2 species among them the pathogenic one is *E. floccosum* (Lakshmipathy and Kannabiran, 2010; Stojanov *et al.,* 2011).

The colonies are slow-growing, the fresh colonies are white and cottony, old culture is powdery and unique brownish yellow in color (Lakshmipathy and Kannabiran, 2010). This genus does not produce microconidia. Macroconidia are abundant and produced singly or in clusters. They are large, multicellular with one to nine septa, club-shaped and thin walled with smooth surface (Weitzman and Summerbell, 1995; Simpanya, 2000; Stojanov *et al.,* 2011). They are 20 to 60 by 4 to 13 mm in size (Weitzman and Summerbell, 1995).

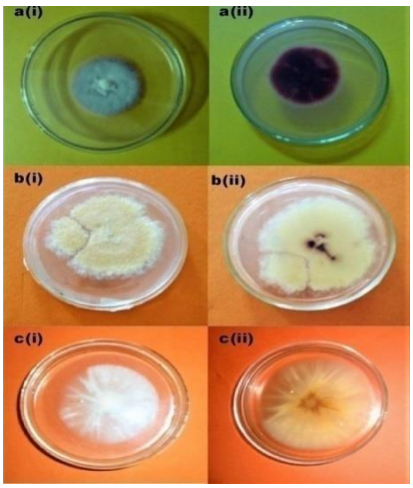

Figure 1: Dermatophyte cultures on SDA medium. a, *Trichophyton rubrum* culture on SDA medium, a(i) Obverse, a(ii) Reverse; b, *Microsporum canis* culture on SDA medium, b(i) Obverse, b(ii) Reverse; c, *Epidermophyton floccosum* culture on SDA medium, c(i) Obverse, c(ii) Reverse.

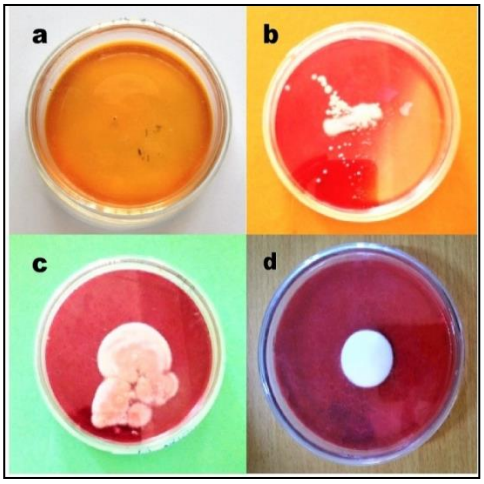

Figure 2: a, Dermatophyte Test Medium (DTM); b, *Trichophyton rubrum* culture on DTM; c, *Microsporum canis* culture on DTM; d, *Epidermophyton floccosum* culture on DTM.

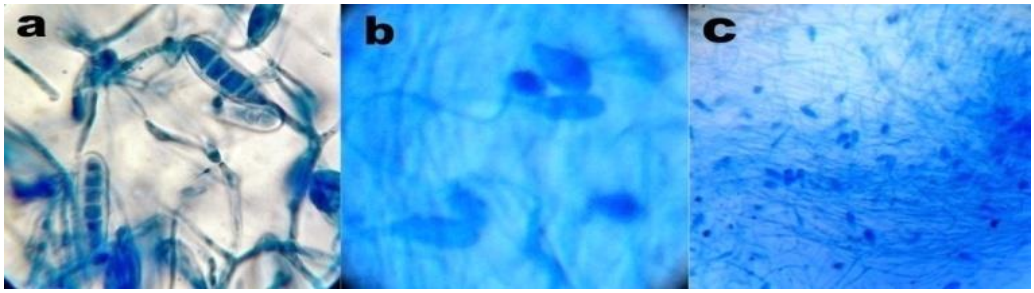

Figure 3: Microscopic view of lacto phenol cotton blue stain wet mount. A, *Microsporum canis* macroconodia under 100X; b, *Epidermophyton floccosum* macroconodia under 40X; c, *Trichophyton rubrum* microconodia under 40X.

EPIDEMIOLOGY AND ECOLOGY

Epidemiology plays an important role in control of infection and public health issues ((Weitzman and Summerbell, 1995). It has been reported that, the frequency of dermatophytosis has changed over the last few years. Several workers reported that *Trichophyton rubrum* is predominantly prevalent species throughout the world (Sharma and Sharma , 2012) . Several workers reported on dermatophytosis from different parts of the country, but there are only few workers reported on the involvement of non dermatophytic fungi and yeast like fungi in superficial mycoses (Hitendra *et al.*, 2012).

The epidemiology of dermatophytoses is influenced by migration, climatic factors, growth in tourism, changes in socioeconomic conditions, overcrowding, healthcare, environmental hygiene, culture and individual characteristics (Ndako *et al.*, 2012; Dehghan *et al.*, 2009; Ameen, 2010). Generally, dermatophytes are cosmopolitan in distribution, that is, they occur in different regions of the world with variations in the frequency of particular species (Peres *et al.*, 2010; Palacio *et al.*, 2000; Dehghan *et al.*, 2009; Seebacher *et al.*, 2002; Segal and Frenkel, 2015). It occurs very commonly in tropical and subtropical countries (Mathur *et al.*, 2012). According to the World Health Organization (WHO), 25% of the world population is affected by dermatophytes. It is estimated that from 30 to 70% of adults are the carriers of these pathogens and that the incidence of the disease increases with age (Seebacher *et al.*, 2002). *T. rubrum* is the most frequent in clinical cases of tinea pedis, tinea unguium, tinea corporis and tinea cruris (Havlickova *et al.*, 2002) . The symptoms and the causative organism of dermatophytosis vary with geographic region, socioeconomic conditions and habits. In developed countries contributing factors to the development of dermatomycoses include animals, increased use of public sports facilities (especially swimming pools), wearing impenetratable training shoes, the increasing incidence of diabetes mellitus

and vascular disease and an ageing population, foot trauma and cigarette smoking.

The dermatophyes are being imported and disseminated by booming mass tourism, international sports activities and increasing migration (Havlickova *et al.,* 2002). The mode of infection may by direct contact or indirect contact. Direct contact with patients and infected pet animals. Swimming pools, seabeaches etc., which could serve as reservoir of skin debris of infected individuals, which could transmit the disease indirectly (Segal and Frenkel, 2015).

In recent decade, the prevalence of dermatophytosis has significantly decreased in many developed nations of the world due to improved social, economic, health care and hygiene practice factors in the former (Ndako *et al.,* 2012).

BIOCHEMISTRY OF PATHOGENESIS

The dermatophytes enter into the host body through injured skin, scars and burns. Either arthrospores or conidia are source of infection. (Lakshmipathy and Kannabiran , 2010). The mannan glycoproteins in the cell wall of the dermatophytes helps in the attachment to the keratin containing epithelial tissue of the host. Although the pathophysiological mechanisms of dermatophytes are poorly studied, it is known that, similar to other filamentous fungi, conidial germination proceeds in three stages: activation, isotropic growth, and polarity growth. Ultrastructure observation of human skin sections during dermatophyte infection revealed that *Trichophyton mentagrophytes* spores attach to the stratum corneum after 12 hours. Lemsaddek et al. (2010) reported that the elongation of the germ tube promotes the invasion and release of several lipolytic and proteolytic exoenzymes, which enter the cornified cells (Lemsaddek *et al.,* 2010). According to numerous reports the pathogenicity of dermatophytes is associated with their synthesis of proteinases, which allow them to feed on keratin and other proteinaceous substrates found in the stratum corneum, nails, and hair (Venkatesan *et al.,* 2002; Samdani, 2005). Numerous proteases have previously been identified from various dermatophyte species and displayed keratinolysis, elastinolysis, and/or collagenolysis activities (Lemsaddek *et al.,* 2010). Proteolytic and keratinolytic activities of dermatophytes have been a subject of interest for several years to understand the pathogenicity of dermatophytosis (Venkatesan *et al.,* 2002). The dermatophyte species within the three genera vary in their pathogenicity *in vivo*. Dermatophytes utilize keratin as a nutrient source; they usually do not invade viable tissue. However, all species colonize and invade the keratinized stratum corneum of the epidermis and the follicular ostium of hairs by secreting exo-enzyme keratinase and induces inflammatory reaction at the site of infection. The ability of different species to penetrate hair and nails varies widely (Lakshmipathy and Kannabiran, 2010; Dueka *et al.,* 2002). Although the causes of this observed tissue specificity are unknown, but are thought to be due to individual organisms requires specific nutritional requirements or the enzyme production (Simpanya, 2000). Fungal conidia adhere to the stratum corneum's underlying substrate and begin to germinate 24 hours later. Ultrastructural observations revealed polymeric material is shown to mediate the adherence between microconidia and stratum corneum cells. As they develop further, germ tubes penetrate horizontally in and through the thickness of stratum corneum and causing skin infections. Invasion of the cornified cells of stratum corneum involves the elongation of the germ tubes by mechanical forces and production of different proteolytic and lipolytic exoenzymes (Straten *et al.,* 2002) . The underlying and surrounding tissues are generally affected due to allergic or inflammatory host responses to the presence of the fungi. Inflammation causes the pathogen to migrate from the site of infection to a new location. This movement results in the classical ringed lesion. As long as the infection continues, the ringed lesion spreads outward (Dueka *et al.,* 2002).

CLINICAL MANIFESTATIONS

Traditionally, the different types of dermatophytosis are classified and have been named according to the anatomic locations involved by using the Latin term designating the body site after the word tinea, e.g., tinea mannum for ringworm of the palm, tinae barbae– stands for the infection of the chin etc., Cutaneous dermatophytosis are usually identified by their scaly patches, with central clearing and sharply demarcated, annular, erythematous, advancing margins, vesicles, blisters and pustules (Stojanov *et al.,* 2011).

Types of dermatophytosis and their clinical manifestations

Tinea capitis

Tinea capitis is the dermatophyte infection of the hair covering the head, eyelashes, and eyebrows, (Weitzman and Summerbell, 1995; Leung *et al.,* 2020). It is predominantly caused by *Microsporum sp.* such as *M, canis* and *M.audouinii* and *Trichophyton tonsurans* (Trovato *et al.,* 2006). Children between the ages of six and thirteen are typically affected with tinea capitis. Symptoms

include alopecia and lymphadenopathia, erythema or severe folliculitis, seborrheic-like scale, 'black dot' pattern and tiny pustules in the scalp (Gupta and Summerbell, 2000). Lesions could be non-inflammatory and persistent, or they could be inflammatory (Hay, 2000).

Tinea corporis

It is the dermatomycosis that appears on body, shoulders and legs. Tinea corporis includes all superficial dermatophyte infections of the glabrous skin, excluding the scalp, beard, face, hands, feet, and groin. (Gupta *et al.,* 2003). Symptoms could be severe with clearly limited erythematous vesicular spots. It is caused by *Microsporum sp, Epidermophyton sp.*and *Trichophyton sp*.

Tinea cruris

It is dermatophytic infection affecting perianal, perineal, genitalia, pubic area, and crotch region. It is commonly seen in older male persons. The symptoms are production of dry dandruff. Causative agents are *T. rubrum* and *E. floccosum* (Weitzman and Summerbell, 1995).

Tinea favus

Tinea favosa is a chronic inflammatory dermatophyte infection of the scalp, glabrous skin, and nails. It is commonly caused by *Trichophyton schoenleinii*. (Anane and Chtourou, 2013). Occasionally, *Trichophpyton. violaceum* or *Microsporum gypseum* may cause similar lesions (Tlamcani *et al.*, 2016). Symptoms could be prominent yellow scabs and dry dandruff (Weitzman and Summerbell, 1995).

Tinea imbricate

It is a chronic infection of skin folds caused by a strictly anthropophilic dermatophyte *T concentricum*. Typically, the symptoms include appearance of several scaly, annular, and concentric rings that can extend to form polycyclic plaques with or without erythema. Later several overlapping lesions develop, and the plaques become lamellar with abundant thick scales adhering to one side, giving rise to the appearance of fish scales or overlapping roof tiles (Leung *et al.,* 2018).

Tinea manuum

Tinea manuum is a dermatophyte infection of the palms and interdigital areas of hands. It can present with erythema and minimal scale on the dorsum of the hand (Tamer and Yuksel, 2017). However, the symptoms of chronic tinea manuum include hyperkeratosis and cracking with or without mild itching of the skin (Tamer and Yuksel, 2017; Errichetti and Stinco, 2018). Its causative agent is *T. rubrum* (Weitzman and Summerbell, 1995).

***Tinea pedis* (Athlete's foot)**

It is the dermatophyte infection of the soles of feet and toes. It is also known as athletes foot. It is the most widely suffered dermatophyte infection. It could be chronic with squamose epithelia, thickening of stratum corneum, redness and inflammation. It is caused by *Epidermophyton floccosum* and *Trichophyton rubrum* (Weitzman and Summerbell , 1995; Johnson , 2002).

***Tinea ungium* (Onychomycosis)**

It is a chronic dermatophytic infection of nails. It appears under nails or superficially (Hasan *et al.,* 2004; Stojanov *et al.,* 2011). It is commonly caused by *T. rubrum* and *T. interdigitale* (Asz-Sigall *et al.,* 2017). It occurs at a higher frequency among the elderly population (Harada, 2011).

Tinea barbae

It is a ringworm of the beard and mustache (Weitzman and Summerbell, 1995). It affects the hairy part of the face – the beard, less often the moustache. It is caused predominantly by zoophilic dermatophytes, but in rare cases, pathogens can be also anthropophilic species, *Trichophyton rubrum* (Vazheva and Zisova, 2021).

CONCLUSION

Dermatophytoses are the most frequent fungal infections all over the world. It affecting individuals in various age groups. Many epidemiological studies have shown that the different forms of tinea are more prevalent in people of low socio-economic status and poor personal hygiene. Improvements in public health care and self-hygiene may play a major role in controlling these diseases.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

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DISCLOSURE OF INTEREST

The authors declare that they have no competing interest.

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